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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Paper No. 28

Application Number: 08/463,904
Filing Date: 6/05/1999
Appellant(s): Joseph B. Phipps

Robert G. Mukai
For Appellant

EXAMINER'S ANSWER

This is in response to appellant's brief on appeal filed March 2, 1999.

(1) Real Party in Interest

A statement identifying the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

A statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief. The examiner requests the Board to review serial number 08/465,492 which the examiner has recently descovered to have overlapping subject matter with the current applicant. The examiner will consider double patenting issues in the event that the examiner is reversed.

(3) Status of Claims

The statement of the status of the claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct. The examiner has allowed applicant's to enter after finals on three separate occasions to better place the case into condition for appeal. This case is a pre-Gatt Treaty application and the examiner has allowed applicant's to amend and restate their case several times to their best position. It is believed that the issues are more clear and that the arguments now correspond to that which is being claimed. As noted by applicant the last after final amendment which is being permitted entry for purposes of appeal is in response the examiner back calculating applicant's concentrations since applicant switched form molarity to mg/ml in their specification and claims (see page 4 of the office action in paper 15) and were claiming concentrations corresponded to a range of 20% efficiency to better when applicant has argued otherwise. The examiner sincerely hopes that all errors have been corrected at this point.

(5) Summary of Invention

The summary of invention contained in the brief appears to venture into issues of opinion and arguments that would be much better presented in applicant's argument section. In order to present to those unfamiliar with the iontophoretic art a clear understanding of the invention as well as what applicant's feel distinguishes over the art, the examiner gives a brief explanation as to the fundamentals of iontophoresis and then contrasts applicant's claimed invention to the fundamentals.

Iontophoresis is an alternative method for delivering drugs to the body wherein the drugs are typically delivered through the skin or mucosal membranes as opposed to oral (pills) and/or subcutaneous (hypodermic/catheter) routes. Typically, a drug that either naturally carries a net charge of either positive or negative in sign, or one that is modified to hold such a charge will be driven into the skin (or other tissue) by placing the drug in a reservoir in contact with an electrode connected to a power source possessing the same charge as the drug. The drug will thus be repelled out of the reservoir by its contact electrode of similar charge and will be attracted to an opposing electrode (a.k.a. counter electrode) placed elsewhere on the skin possessing an opposite charge. The drug ions can be thought of as serving to complete the circuit and to carry charge from one electrode to the other much as the electrons in a closed electrical circuit. Such an arrangement of device and corresponding method of delivery have been conventional in the art for well over 100 years.

Applicant's presently claimed invention is directed to the delivery of the drug fentanyl

as modified into a charged form, namely fentanyl salt. The iontophoretic delivery of fentanyl salt to induce analgesia has been disclosed and claimed in commonly owned USPN 5,232,438 in particular reference to claims 1 and 20 which claim an article and method of inducing analgesia in a patient by delivering fentanyl salt at a rate sufficient to induce analgesia. Thus, with all other limitations of the presently claimed method and apparatus having been demonstrated, applicant's wish to hinge "patentability"upon specified concentration range of the drug, namely "above about 16 mM". Applicant's feel that as a result of their having tested the delivery of fentanyl (see figure 2 of the application) for determination of the optimum range of drug concentration, that their claiming of that range should be recognized as patentable material. To the contrary, it is the examiner's position that the determination of such a range has long been held to be an obvious optimization of ranges in accordance with MPEP 2144.05.

(6) Issues

The appellant's statement of the issues in the brief is incorrect.

As the result of the examiner's permitting applicant claim 13 is now broader in scope than it's independent claim 10 causing a new grounds of rejection under 112 second paragraph.

(7) Grouping of Claims

The rejection of claims 1, 4, 7-10, 13, 16-17 stand or fall together because appellant's brief does not include a statement that this grouping of claims does not stand or fall together and reasons in support thereof. See 37 CFR 1.192(c)(7).

The provisions for the appeal process have particularly set aside this section for grouping of claims (as opposed to the argument section) to let applicant present clear definitive reasons as to whether or not a line of demarcation exists within the claims on appeal of inventions that are to be treated as patentably distinct. This simple task of invention summary gives the examiner a chance to respond to such reasoning and aid in the board's determination of patentability. Too often, in recent appeals experienced by this examiner, the applicant has placed that burden back upon the office to determine those lines by the statement "for reasons that will later become apparent". The examiner sees this as a mere waiving of the opportunity afforded to applicant to briefly explain those differences.

(8) Claims Appealed

The copy of the appealed claims contained in the Appendix to the brief is correct.

(9) Prior Art of Record

The following is a listing of the prior art of record relied upon in the rejection of claims under appeal.

5,125,894	Phipps et al	June 30,1992
5,203,768	Haak et al	April 20, 1993
5,423,739	Phipps et al.	June 13, 1995

(10) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 112

Claim 13 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. As noted above, applicant's amendment to independent claim 10 is narrower in scope than claim 13. Applicant argues that claim 10 corresponds to concentrations greater than 6mg/ml, yet claim 13 claims 5/ mg/ml which the examiner notes is in the lower efficiency range on figure 2 than argued by applicant.

Claim Rejections - 35 USC § 103

Claims 1, 4, 7-10, 13, 16-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Phipps et al '739 in view of Phipps '894.

Primary reference Phipps et al '739 teaches the delivery of fentanyl and sufentanil (column 13 line 50) in hydrogels (see last line of abstract) which may comprise an adhesive (column 6 lines 18-20). Applicant differs in reciting a specific range of concentration for fentanyl to render the drug flux independent of the concentration of the medicament in the reservoir. Secondary reference Phipps et al USPN 5,125,894 discusses the relationships between current intensity and density and drug concentration in general and how medicaments have a threshold level above which, a linear relationship exists between current levels and the amount of drug

delivered. Phipps et al refer to the Padmanabhan article (a copy of which applicant has supplied in the response of 6-9-97) which demonstrates the relationship for a particular compound and system. Since Phipps '894 teaches that it was desirable to deliver medicaments above their threshold level (and supposedly even during the addition of extraneous ions) so that the amount of current can be utilized to control the rate of drug delivery over a sustained period of time. To have tested, determined and used the threshold levels for fentanyl and sufentanil in a particular systems that include (or don't include) extraneous ions would have been an obvious optimization of parameters to sustain desired levels of drug flux.

1. Claims 1, 4, 7-10, 13, 16-17 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Haak et al USPN 5,203,768 (in view of Phipps '894). Haak et al is owned by the Alza corporation, the appellant in this appeal. Haak et al provides working examples of fentanyl in a hydrogel which are stated to provide 25 ug of fentanyl and 5 ug of sufentanil every 5 minutes that the device is in activation. Since the device must act in a linear fashion for patentee to make this statement, it is inherent that the concentration is in the range claimed by applicant. Notwithstanding, a 10% concentration of fentanyl is incorporated into the patch. Thus, even if the gel, when hydrated, absorbs twice its weight in water, the concentration of fentanyl will still be 1% of the solution and three times the minimal concentration provided by the claim. Since applicant appears to have a common assignee and have access to these gels the examiner requests hydration data and other related material that may provide

information about the drug concentrations in these examples. Haak teaches that the device is turned on during episodes of pain (i.e. turned on and off), thus a "substantial" portion of the drug remains in the reservoir when the device is intermittently turned off. If not inherent, it would have been obvious in view of Phipps "894 to have operated the device in the linear region for fentanyl which would inherently include at least a portion of applicant's claimed range.

It is noted that buffering the solutions is considered an option (see column 6, lines 1-8)

(11) Response to Argument

As noted above in the summary of the invention, the difference between the prior art and the claims is that applicant has claimed a range of use for the drug. The examiner maintains that the drug range was a mere routine determination of obvious parameters. The examiner also requests the Board to review the examiner's final rejection in its entirety in case the examiner has failed to reiterate points of argument. It is believed that the Phipps declaration was best treated therein.

To demonstrate the above statement the examiner has cited patent No. 5,232,438 and particularly claim 20 of the patent. A reading of the patent reveals that the disclosure was directed to particular membranes that mimic the skin. The patentee owner, The Alza corporation, who happens to be the appellant in this particular application as well, tested the membranes (not in vivo) for metoclopramide and then speculated that the drug fentanyl would work as well. There is no explicit teaching of any method of fentanyl delivery, however it did

not prevent the patentee from claiming a method of inducing analgesia in a patient. The '438 patent is the subject of reexam 90/003535 which is still pending. The patentees have maintained that the claims are supported by the disclosure and that "unexpected" results where found in the method of inducing analgesia. The reexam is still pending, however the application is missing and an official search is now being conducted to locate the file. The examiner believes the Board may wish to review the arguments in this file and the examiner will be happy to provide such upon being located.

In the current application the appellants have finally provided some examples and have determined the minimum value at which fentanyl should be delivered. The examiner believes that the following in depth arguments are really not necessary. MPEP 2144.05 has long provided that the mere optimization of desirable parameters is reasons for denying a patent under 35 USC 103. The examiner believes that to one of ordinary skill in the art, a pharmacist of 4 years of college and 4 years of medical school, that setting dosages extremely important and that drug delivery efficiency are well known parameters to optimize. If fact, the examiner believes that in all aspects of business as well as engineering, maximizing efficiency is a given when it comes down to testing. The examiner believes that these facts would alone be grounds for denying appellant's the current claims under 35 USC 103.

In fairness to the appellant, the examiner has made an evidentiary showing that efficiency was indeed known in the iontophoresis art and further that a linear relationship between current and concentration was desired to better control drug quantities. The examiner

has relied upon the words of appellants own inventor Phipps ' 739 to demonstrate that it was known that drugs typically have a threshold level in terms of concentration before a linearity between current and concentration is found.

The appellant's have taken the position that one of ordinary skill in the art has no more information to him than what exists in the patents before him. The examiner finds it preposterous for appellant to assume that the ordinary skilled pharmacist would not factor toxicity into the equation for determining dosage settings. The examiner also finds it preposterous that appellants argues that part of there invention is to prevent unintentional overdosages when the upper limit of their claim ranges are unbounded. The examiner refers to pages 7-15 of the office action of 4-2-98 for a full treatment of the Phipps declaration.

The appellants have now tried to down play the significance of the Phipps '739 remark and have stated the examiner has "clung to a single statement of the '894 patent" to rebut the argument and despite the fact that one of their own inventors made the statement still will not acknowledge that threshold levels where not commonly known and a desirable value to operate. The examiner has other evidence to support that threshold values were of concern to the artisan. As appellant well knows, during the reexamination of a competitor inventor's (Petelenz's USPN 4,752,285), a translation of from a Russian textbook emerged as casting doubt upon the Petelenz claims. Unfortunately the examiner cannot find the publication date of this reference but will pursue such if appellant's challenge its authenticity or it's availability as prior art. It is believed from the examiner's recollection that the reference has a publication

date of somewhere in the 1950's .The examiner notes that this reference was cited in the reexams, which were open to the public, well before applicant's filing date. The examiner refers to such as the Allen translation which a copy of is attached hereto. The "allen translation" discusses a study undertaken to establish the relationship between concentration and current (see page 13, next to last paragraph.

Some of the relevant conclusions are found on pages 20, 25, 29 as highlighted by the examiner. On page 25, it was found that the amount of substance delivered was directly proportional to the quantity of electricity applied (i.e. a linear relationship was established) significance of this is "The amounts of substance introduced (p/g) listed in the table in terms of milligrams per coulomb can be used by the physician- physiotherapist in his practical and scientific work, since the number of coulombs transferred during the procedure can readily calculated from the current strength and time". However, there are exceptions to this rule, see page 20. "The amount of the major ion falls off sharply both with an increase in the concentration of the parasitic ion and with a decrease in the concentration of major ion". In other words, if you use a dilute solution of the major ion, other ions in the solution will start to compete for transfer and the linearity (efficiency) of delivery falls off. This is totally consistent with the statement in the Phipps '894 reference concerning linearity and threshold of drugs and current despite the Phipps declaration denial of such.

In conclusion, as noted above, without even going into the details of threshold values, the mere optimization of drug delivery for reliabilty is obvious. The FDA requires such prior to putting device for delivering drugs on the market. To the best of the examiner's recollection, appellant's argued that they were seeking FDA approval for the subject matter of the aforementioned 90/003535 reexam. However, even more so, appellant's own words as well as the evidence on the record show that linearity (see Allen translation) was a desirable parameter for accuracy in delivering drugs.

Respectfully submitted,

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PRIMARY EXAMINER

MWB
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